

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of

Dario NERI et al

Serial No.: 09/300,425

Filed: April 28, 1999

For: SPECIFIC BINDING MOLECULES FOR SCINTIGRAPHY, CONJUGATES
CONTAINING THEM AND THERAPEUTIC METHOD FOR TREATMENT
OF ANGIOGENESIS

BOX: SEQUENCE

Group Art Unit: 1645

Examiner: V. Portner



#14B 9/16/00
T. Gray

AMENDMENT IN RESPONSE TO NOTICE UNDER 37 C.F.R. §1.821-§1.825

Commissioner for Patents
Washington, DC 20231

Sir:

In response to the Notice to Comply With Requirements for Applications Containing Sequence Disclosures mailed August 1, 2000 (Paper No. 12), please delete the previously filed Sequence Listing (submitted on May 21, 1999), enter the Amended Sequence Listing filed concurrently herewith, and amend the application as follows:

IN THE SPECIFICATION:

Page 3, line 18, after "(3)" insert --(SEQ ID NOS 22-24, respectively)--.

Page 9, line 31, after "library" insert --(SEQ ID NOS 11-18, respectively)--.

Page 10, line 7, after "L19" insert --(SEQ ID NOS 19-21, respectively)--.

Page 14, line 12, after "390" insert --(SEQ ID NOS 25-26, respectively)--.

Page 17, line 28, after "LMB1bis" insert --(SEQ ID NOS 1-2, respectively)--.

Page 18, line 1, after "DP47CDR1back" insert --(SEQ ID NOS 3-4, respectively)--.

line 6, after "DP47CDR2back" insert --(SEQ ID NOS 5-6, respectively)--.

line 27, after "DPKCDR1for" insert --(SEQ ID NO: 7)--.

Page 18, line 30, after "DPKCDR1back" insert --(SEQ ID NOS 8-9, respectively)--.

Page 19, line 3, after "DPKCDR2back" insert --(SEQ ID NO: 10)--.

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21. (Amended) A conjugate according to claim 20 wherein the molecule which induces blood coagulation and blood vessel occlusion is a photoactive molecule.

22. (Amended) A conjugate according to claim 21 wherein the photoactive molecule is a photosensitizer.

23. (Amended) A conjugate according to claim 22 wherein the photosensitizer absorbs at a wavelength above 600 nm.

24. (Amended) A conjugate according to claim 22 wherein the photosensitizer is a derivative of tin (IV) chloride.

Please add new claims 28-39 as indicated below.

-- 28. A conjugate according to claim 20, wherein said affinity is in the subnanomolar range.

29. A conjugate according to claim 28 wherein the molecule which induces blood coagulation and blood vessel occlusion is a photoactive molecule.

30. A conjugate according to claim 29 wherein the photoactive molecule is a photosensitizer.

31. A conjugate according to claim 30 wherein the photosensitizer absorbs at a wavelength above 600 nm.

32. A conjugate according to claim 30 wherein the photosensitizer is a derivative of tin (IV) chloride.

33. A conjugate according to claim 20, wherein the antibody is an scFv antibody.

34. A conjugate according to claim 33, wherein the antibody is a recombinant antibody.

35. A conjugate according to claim 33, wherein the antibody comprises a limited number of mutations in its CDR residues.

36. A conjugate according to claim 35, wherein the mutated residues are residues 31-33, 50, 52 and/or 54 of its VH domain and/or residues 32 and/or 50 of its VL domain.

37. A conjugate according to claim 28, wherein the antibody binds to the ED-B domain of fibronectin with a K_d of about 54 pM.

38. A conjugate according to claim 28 with the following amino acid sequence

vH (SEQ ID NO: 19)

EVQLLES GGG LVQPGGSLRL SCAASGFTFS
SFSMSWVRQA PGKGLEWVSS ISGSSGTTY
ADSVKGRFTI SRDNSKNTLY LQMNSLRAED
TAVYYCAKPF PYFDYWGGGT LVTVSS

linker (SEQ ID NO: 20)

GDGSSGGSGGASTG

vL (SEQ ID NO: 21)

EIVLTQSPGT LSLSPGERAT LSCRASQSVS
SSYLAWYQQK PGQAPRLLIY YASSRATGIP
DRFSGSGSGT DFTLTISRLE PEDFAVYYCQ
QTGRIPPTFG QGTKVEIK

39. A conjugate according to claim 20, wherein said affinity is about 0.05 nM. --
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L V Q P G G S L R L
P G K G L E W V S S
S R D N S K N T L Y
P Y F D Y W G Q G T

S C A A S G F T F S
I S G S S G T T Y Y
L Q M N S L R A E D
L V T V S S

W

G D G S S G G S G G A S T G

19

P E D F

19

E I V L T Q S P G T
S S Y L A W Y Q Q K
D R F S G S G S G T
Q T G R I P P T F G

L S L S P G E R A T
P G Q A P R L L I Y
D F T L T I S R L E
Q G T K V E I K

L S C R A S Q S V S
Y A S S R A T G I P
P E D F A V Y Y C Q

Figure 6: Amino acid sequence of antibody L19

[illegible]